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The purpose of this study was to compare bone densitometry to quantitative ultrasound (QUS) and to assess gender differences in a young healthy population. Seventy-five active, aged-matched (~29 yrs) men (N = 29) and women (N = 46) were assessed for bone mineral density (BMD, g/cm2) and broadband ultrasound attenuation (BUA, db/MHz). BMD of the total body, regional and lumbar spine was measured via dual-energy X-ray absorptiometry (DXA), and BUA was measured using the QUS-2Ô ultrasonometer. Data analysis included Pearson product-moment to compare DXA to QUS, and receiver operating characteristic (ROC) curves and Kappa coefficients for discrimination of the two procedures. There was no significant gender difference in lumbar spine (LS) BMD. Regional and total body BMD and BUA were greater for men than women. Total body BMD (mean ± SD) for men was 1.29 ± 0.09 g/cm2 and for women was 1.22 ± 0.07 g/cm2. BUA (mean ± SD) was 107.0 ±16.7 db/MHz vs. 97.8 ± 11.6 db/MHz for men and women, respectively. All BMD sites except LS and pelvis were significantly correlated to BUA for men (r = 0.46-0.48), but only LS (r = 0.32) and arms (r = 0.30) were significantly correlated to BUA for women. Kappa coefficients ranged from -0.09 to 0.17 for men, none of which were significant, and the range for women was 0.09 to 0.25 with pelvis and legs attaining significance. There was low percent agreement between QUS and DXA (28%-45% for men and 41%-50% for women), and the area under the curve (AUC) derived from ROC analysis resulted in little discrimination (AUC = 0.60-0.64). Our results showed little agreement between DXA and QUS; therefore, QUS would not be a surrogate indicator for the measurement of BMD by DXA. These results indicate that QUS measures different aspects of bone health and may complement the use of DXA.

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ASSESSMENT OF BONE HEALTH IN MEN AND WOMEN COMPARING DXA TO CALCANEAL ULTRASOUND

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The investigators have adhered to the policies for protection of human subjects as prescribed in Army Regulation 70-25, and the research was conducted in adherence with the provisions of Title 45 Code of Federal Regulations Part 46.

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EXECUTIVE SUMMARY

The purpose of this study was to compare bone densitometry to quantitative ultrasound (QUS) and to assess gender differences in a young healthy population. Seventy-five active, aged-matched (~29 yrs) men (*N* = 29) and women (*N* = 46) were assessed for bone mineral density (BMD, g/cm^2) and broadband ultrasound attenuation (BUA, db/MHz). BMD of the total body, regional and lumbar spine was measured via dual-energy X-ray absorptiometry (DXA), and BUA was measured using the QUS-2™ ultrasonometer. Data analysis included Pearson product-moment to compare DXA to QUS, and receiver operating characteristic (ROC) curves and Kappa coefficients for discrimination of the two procedures. There was no significant gender difference in lumbar spine (LS) BMD. Regional and total body BMD and BUA were greater for men than women. Total body BMD (mean ± SD) for men was 1.29 ± 0.09 g/cm^2 and for women was 1.22 ± 0.07 g/cm^2. BUA (mean ± SD) was 107.0 ± 16.7 db/MHz vs. 97.8 ± 11.6 db/MHz for men and women, respectively. All BMD sites except LS and pelvis were significantly correlated to BUA for men (r = 0.46-0.48), but only LS (r = 0.32) and arms (r = 0.30) were significantly correlated to BUA for women. Kappa coefficients ranged from -0.09 to 0.17 for men, none of which were significant, and the range for women was 0.09 to 0.25 with pelvis and legs attaining significance. There was low percent agreement between QUS and DXA (28%-45% for men and 41%-50% for women), and the area under the curve (AUC) derived from ROC analysis resulted in little discrimination (AUC = 0.60-0.64). Our results showed little agreement between DXA and QUS; therefore, QUS would not be a surrogate indicator for the measurement

of BMD by DXA. These results indicate that QUS measures different aspects of bone health and may complement the use of DXA.

INTRODUCTION

Low bone mass has been demonstrated to be predictive of those at risk for stress fracture (10). Although stress fractures often occur in elderly, osteoporotic individuals, certain young populations are at risk as well. These populations include athletes participating in weight-bearing sports (5) and military personnel undergoing prolonged physical training (2, 9). In these instances, stress fractures result from the inability of bone to withstand the repetitive weight-bearing loads of physical training. In order to identify those at risk of developing stress fractures, an accurate measurement of bone health is required. Traditionally, bone mineral density (BMD) as measured by dual energy X-ray absorptiometry (DXA) has been accepted as the gold standard for assessing bone health. However, alternative techniques need to be assessed, such as quantitative ultrasound (QUS), which give additional information of bone strength and quality and are more field expedient.

The measurement of QUS yields the parameter broadband ultrasound attenuation (BUA). A pulse of ultrasonic waves is passed through the calcaneus, and the attenuation of the signal is measured. Low BUA indicates a low bone mass. In the current literature, QUS has been shown to be predictive of stress fracture in an elderly population (18, 31) and in the military (22), as well as identifying those at risk for osteoporosis (11, 25). These relationships are independent of BMD and are comparable to those of densitometry. After adjusting for BMD, the predictive quality of QUS still exists (3). Most of these studies have been performed on elderly

postmenopausal women. The utility of QUS for measuring bone health in young, active men and women has not been fully identified in the literature.

There are several advantages to using QUS for measuring bone health. It is small, portable, less costly and radiation-free, which facilitates the rapid screening of large groups of people. These characteristics are ideal for clinical and military settings. In the military, the incidence of lower extremity stress fracture has been documented at 3%-10% (2, 4); therefore, the ability to identify those at risk could initiate early intervention resulting in substantial cost savings to the military. Another advantage to QUS is the ability of BUA to provide additional information about the structure and strength of bone (14). The attenuation of the ultrasonic signal is thought to reflect not only bone mass, but also the bone geometry and composition. If this claim were true, we would not expect QUS and DXA measurements to be highly correlated.

The incidence of stress fracture during military training is generally twice as frequent in women than in their male cohorts and can have an incidence of up to 10% (10). The need exists to identify bone health differences between genders and to develop accurate methods of identifying those with sub-optimal bone health parameters. The objective of this study was to compare calcaneal QUS with regional and total body DXA measurements and to assess these values in a population of age-matched healthy, active, young men and women.

METHODS

TEST VOLUNTEERS

Seventy-five men (N = 29) and women (N = 46) from the West Point Class of 1993 were recruited 6 years after graduation to participate in this study. Mean age was 28.9 ± 0.7 years for men and 28.6 ± 0.7 years for women. All women were premenopausal. The volunteers were briefed on the procedures and signed an informed consent form. Subjects were medically cleared by a physician prior to the study and were not on any medications, other than oral contraceptives, that are known to affect bone metabolism.

CALCANEAL ULTRASOUND

BUA ($dB \cdot MHz^{-1}$) was measured on the right heel using the QUS-2 ™ calcaneal ultrasonometer (Quidel, San Diego, CA) according to manufacturer's specifications. BUA is the parameter of choice when using the QUS-2 because it is more consistently associated with fracture risk (17). The subject sat in a chair while placing the right bare heel between the motorized scanning transducers, which automatically find the posterior, inferior calcaneus. Only the right heel was measured because previous studies have shown bilateral symmetry of the calcaneus in the absence of pathology (30, 32). Figure 1 depicts the procedure. This method is considered a "dry" procedure because it uses an aqueous-based gel as the coupling agent, as opposed to a water immersion technique. Two subsequent BUA measurements were taken in order to determine the reliability of the measurement. The regression of duplicate measurements yielded a correlation coefficient of 0.98, and the coefficient of variation was < 2.6%.

BONE MINERAL DENSITY

Total body and regional (spine, pelvis, legs, ribs and arms) BMD were assessed by DXA (model DPX-L system 7369, Lunar Corp., Madison, WI) using software version 1.35. In addition, the lumbar spine was measured while the subject lay on the DXA table in a supine position with legs bent at 90° for a 2-minute radiological scan as shown in Figure 2. A trained and credentialed technician performed all scans. The short-term (24 hr) coefficient of variation for BMD measurements in our laboratory was < 2.7%.

Figure 1. Calcaneal ultrasound device (QUS-2 ™, Quidel, San Diego, CA).

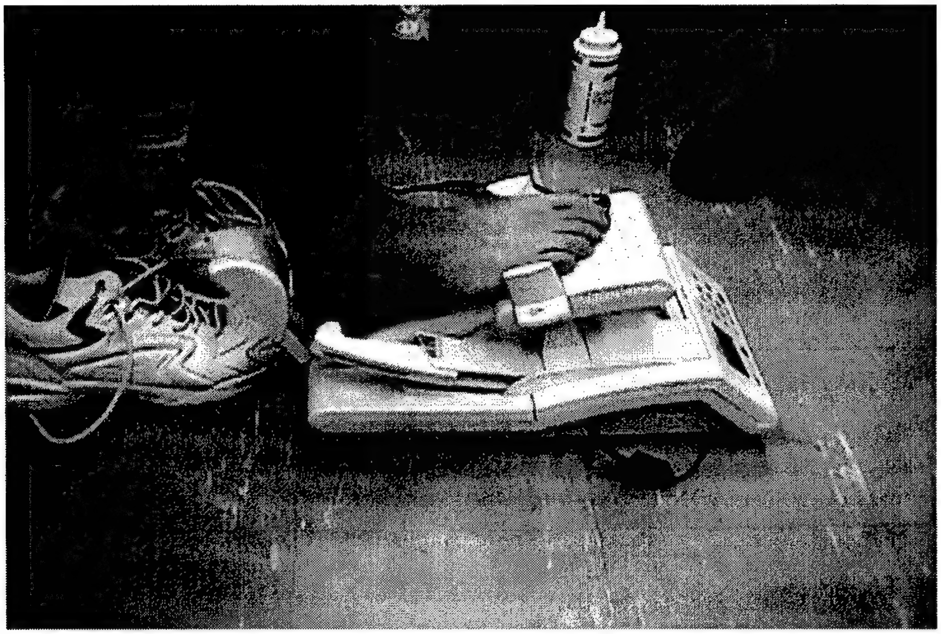
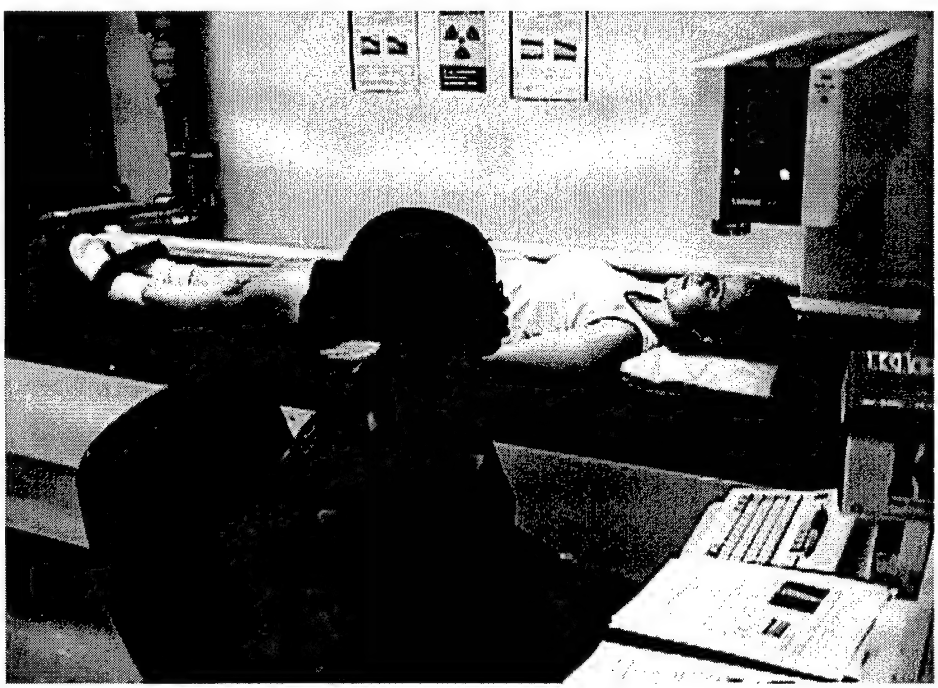


Figure 2. DXA apparatus.



STATISTICAL ANALYSIS

The data were analyzed using the Statistical Package for the Social Sciences (SPSS Inc, Chicago, IL), Statistical Analysis System (SAS Institute Inc., Cary, NC) and STATA (Stata Press, College Station, TX). An independent t-test was used to determine gender differences in descriptive statistics. Pearson product-moment correlation was used to determine test-retest reliability of BUA and to compare BUA to total body and regional BMD sites.

Kappa coefficients (6) were calculated to measure the degree of agreement between BMD from the DXA and BUA from QUS. Both the ultrasound and DXA measurements were categorized into tertiles, representing low, middle and high measures of bone density. Tertiles were calculated separately for gender specific analysis. Agreement between these tertiles was then compared via the Kappa coefficient using STATA V6 software. Receiver operating characteristic (ROC) curves were utilized to determine the discrimination between the BUA and regional DXA measurements. The ROC curve is a measure of sensitivity versus 1-specificity throughout the range of data (27). Sensitivity refers to the proportion of observed positive outcomes that are correctly classified and specificity refers to the proportion of observed negative outcomes that are correctly classified. The median value of total body and lumbar spine BMD was used to categorize subjects into "low" or "high" bone density groups. This dichotomous variable was used as the dependent variable in a logistic regression analysis against QUS. Sensitivity and 1-specificity were calculated throughout the range of each QUS measure to construct the ROC curve. The area under the curve (AUC) was then calculated where an AUC of 1.0 suggests a perfect model (perfect discrimination), and an AUC of 0.5

suggests no predictive power (no discrimination). This analysis was conducted on each gender separately where the gender-specific median values were used. SPSS was utilized to construct the ROC curves and AUC calculations. Level of significance for all tests was set at an alpha level of 0.05.

RESULTS

Table 1 shows the subject characteristics of men and women. Women were significantly shorter and lighter with a lower fat free mass and a higher percent body fat and fat mass. Figures 3 and 4 show a gender comparison of BMD and BUA, respectively. Men had a significantly ($P<0.05$) higher BMD than women for all sites except the lumbar spine and total spine. Men also had a significantly ($P<0.05$) higher BUA than women.

Table 1. Volunteer Characteristics. (Mean ± SD and Range) *$P<0.001$

	Men (N=29)	Women (N=46)
Age (yr)	28.9 ± 0.7 (28.1 – 31.1)	28.6 ± 0.7 (27.4 – 31.5)
Height (cm)	174.7 ± 6.6 (161.8 – 189.5)	167.1 ± 5.6* (155.4 – 179.6)
Weight (kg)	79.8 ± 10.3 (60.9 – 103.6)	66.5 ± 8.8* (53.3 – 94.2)
Body Fat (%)	18.1 ± 5.4 (8.1 – 29.9)	26.2 ± 5.1* (19.5 – 38.8)
Fat Free Mass (kg)	65.2 ± 6.8 (55.0 – 85.0)	48.7 ± 3.9* (41.7 – 58.0)
Fat Mass (kg)	14.6 ± 5.6 (4.9 – 30.6)	17.8 ± 5.8* (11.2 – 36.5)

Figure 3. Regional and total BMD for men and women. (Mean ± SE *P <0.05)

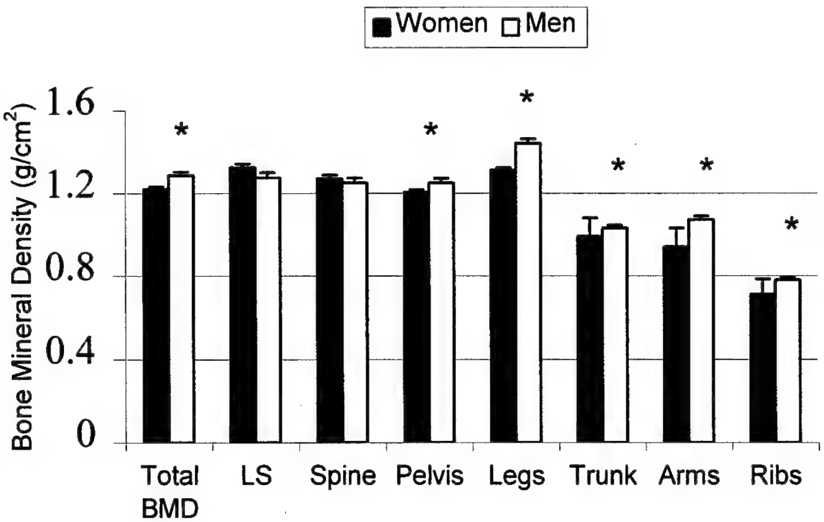


Figure 4. BUA values for men and women. (Mean ± SE *P <0.05)

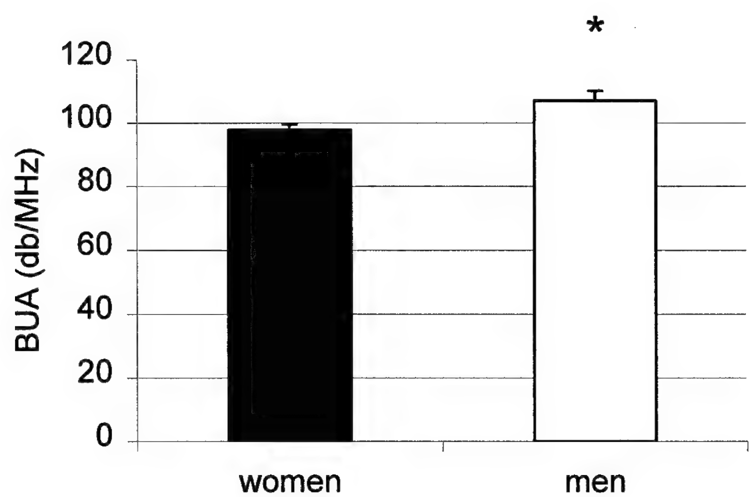


Table 2 shows the correlation coefficients of BUA with total and regional BMD by DXA. In men, the BUA had moderate predictive value (r = 0.35 – 0.48), which was significant ($P < 0.05$) for BMD at all sites except the pelvis. In women, BUA correlated significantly ($P < 0.05$) for the lumbar spine (r = 0.32) and arms (r = 0.30) only.

Table 2. Correlation Matrix between BUA and BMD by DXA. (*P<0.05; **P<0.01)

	Total BMD	LS	Spine	Pelvis	Legs	Trunk	Arms
Total Population (N=75)	0.45*	0.25*	0.31*	0.34*	0.43*	0.43*	0.50*
Men (N=29)	0.48**	0.35	0.46*	0.36	0.46*	0.47*	0.48**
Women (N=46)	0.25	0.32*	0.25	0.19	0.19	0.27	0.30*

Kappa coefficients and percent agreement between BUA by QUS and BMD by DXA are shown in Table 3. Kappa Coefficients for men ranged from –0.09 to 0.17, none of which were statistically significant. Percent agreement for men ranged from 28%-45% for the various BMD sites. Kappa coefficients for women ranged from 0.09 to 0.25 with pelvis BMD and legs BMD attaining statistically significance at $P< 0.01$ and $P<0.05$, respectively. Percent agreement ranged from 39%-50% for women.

Table 3. Kappa coefficients and percent agreement between BUA and BMD sites. A coefficient of +1 indicates complete agreement; whereas a coefficient of –1 indicates complete disagreement. (**P*<0.05, ***P*<0.01)

BMD site	Total Population		Men		Women	
	Kappa Coefficient	% Agreement	Kappa Coefficient	% Agreement	Kappa Coefficient	% Agreement
Total BMD	0.10	40%	-0.09	28%	0.12	41%
LS	0.10	40%	0.12	42%	0.15	43%
Spine	0.14*	43%	0.17	45%	0.18	46%
Pelvis	0.14*	43%	0.12	41%	0.25**	50%
Legs	0.00	33%	0.17	45%	0.22*	48%
Trunk	0.08	39%	0.17	45%	0.11	41%
Arms	0.10	40%	-0.08	28%	0.09	39%
Ribs	0.12	41%	0.11	41%	0.09	39%

The ROC curve analysis was performed for total body BMD and LS BMD, as shown in Figures 5 through 8. The AUC for total body BMD and LS BMD was 0.65 and 0.60 for men and 0.54 and 0.62 for women, respectively. These results demonstrate little discrimination exists between total body BMD, LS BMD and QUS measurements.

Figure 5. ROC curve for women QUS vs. lumbar spine BMD. AUC = 0.62

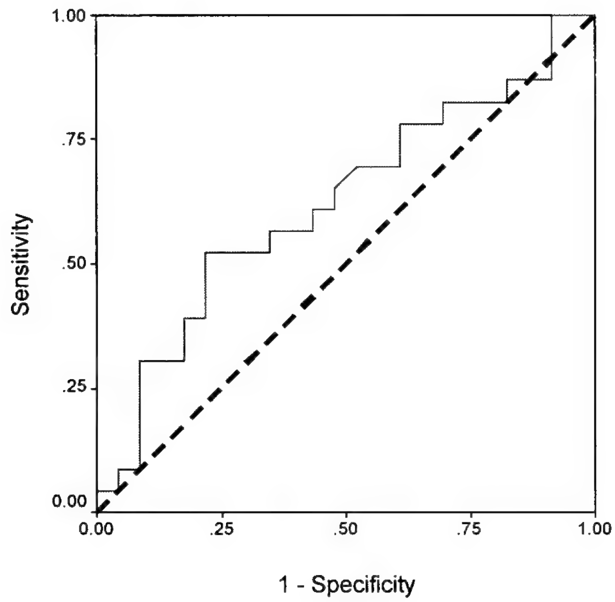


Figure 6. ROC curve for women QUS vs. total body BMD. AUC = 0.54

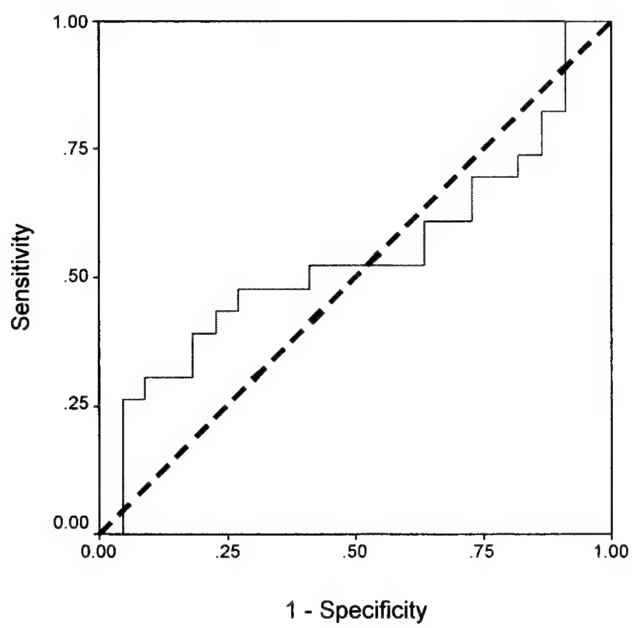


Figure 7. ROC curve for men QUS vs. lumbar spine BMD. AUC = 0.60

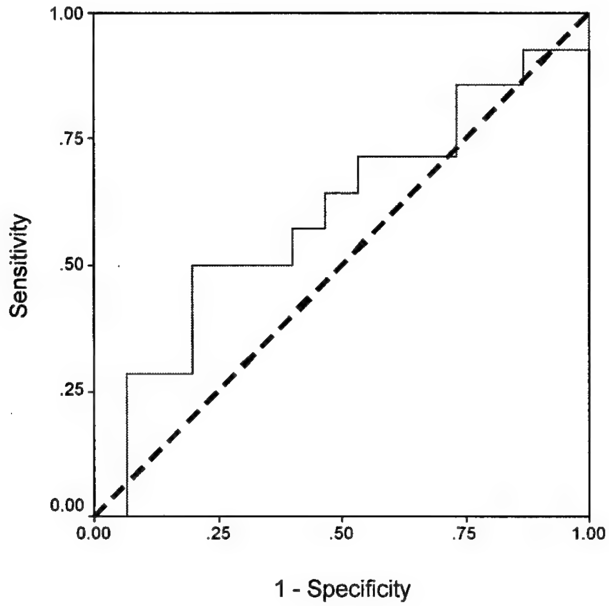
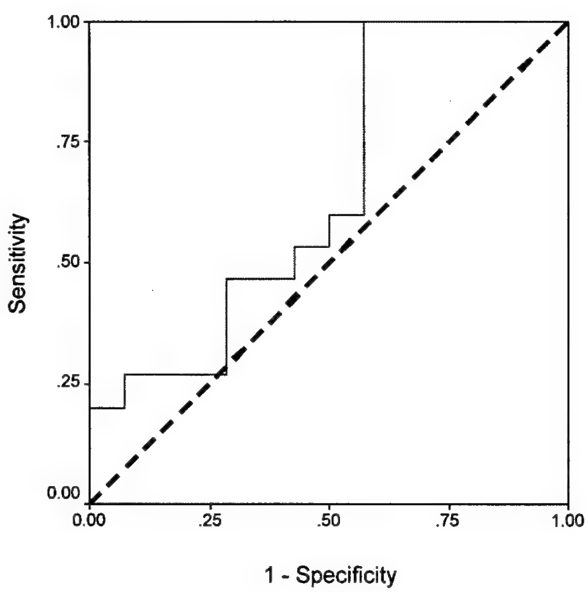


Figure 8. ROC curve for men QUS vs. total body BMD. AUC = 0.65



DISCUSSION

The primary objective of this study was to investigate the relationship between DXA and QUS in order to determine the efficacy of utilizing QUS as a field expedient screening tool to measure bone density. It is important for physically active populations to maintain bone health early in life and to identify those who may be at risk for stress fracture so that early intervention may take place. The QUS may also play a role in monitoring the response of bone to those interventions. In the recent literature, however, a wide range of correlations and discriminative values has been reported comparing QUS parameters to BMD by DXA (3, 17, 18, 30, 33) .

The correlations between BUA and various BMD sites yielded moderate ($r = 0.19\text{-}0.50$) but significant ($P < 0.05$) relationships. Only 4%-25% of the variation in BMD can be explained by the measurement of BUA. Our results are supported by those of Rosenthall et al. (29) who found correlation coefficients of ~0.45 between BUA and the lumbar spine, femoral neck, and Ward's triangle BMD, respectively, in premenopausal women. Taaffe et al. (32) also reported correlations coefficients of ~0.56 for BUA and lumbar spine, femoral neck, trochanter, Ward's triangle and total body BMD, respectively, in women aged 19. In another group of premenopausal women, Dubois et al. (7) found correlation coefficients of 0.51, 0.31 and 0.38 between BUA and lumbar spine, total hip and femoral neck BMD, respectively. In addition, Langton et al. (25) found correlations of 0.35 and 0.40 for BUA and femoral neck and spine, respectively, in perimenopausal women. Based upon our findings, which are supported by these studies, we conclude that the QUS measurement of BUA at the heel is only moderately

predictive of BMD at other skeletal sites in young adults. Therefore, substitution of QUS for the DXA in determining bone mineral density should be used with caution.

In order to further examine the relationship between BUA and the various BMD sites, Kappa coefficients were calculated and percent agreement determined. The Kappa coefficients were only significant for pelvis BMD and leg BMD for women, and percent agreement was not greater than 50% for any regional BMD site. In addition, the AUC determined from the ROC curves ranged from 0.58-0.64 showing little discrimination between tests. These results are in contrast to those observed by Taaffe et al. (32) who studied DXA and QUS in 19-year-old college gymnasts and physically active controls. They found a higher AUC (0.75-0.87) and a higher percent agreement (61%) by Kappa coefficient. Their results may differ from ours due to differences in physical training and age of subjects.

The moderate association between BUA and BMD may exist because ultrasonography measures other bone strength parameters in addition to mineral density. It is thought that BUA is a measure of bone microarchitecture, such as the number and orientation of the trabeculae, which is considered reflective of bone quality. Using radiographs and high-resolution 3-D microcomputed tomography, Glüer et al. (15) found that BUA was associated with trabecular orientation, spacing and connectivity. They postulated that BUA measures different skeletal properties than mineral density (14). The calcaneus is 90% trabecular bone, and BUA is highly correlated to trabecular bone volume in cadavers ($r = 0.99$) (1). Trabecular bone changes in response to

compression or tensile force more so than compact bone; therefore, it is possible that BUA may be a more specific measure of trabecular separation, which occurs with osteoporosis. Dubois et al. (7) found weaker correlations between BUA and femoral neck and total hip BMD in premenopausal women compared to postmenopausal women. They speculated that BUA is relatively insensitive to detecting low BMD when the microarchitecture is still intact, such as in younger premenopausal populations. This interpretation would also help explain the moderate correlations reported herein indicating that BUA may assess bone quality independent of BMD.

Another source contributing to lack of predictive power between BUA and BMD measurements may reside in the region of interest (ROI) studied. In order to test the effect of ROI, Langton et al. (24) performed site-matched measurements of calcaneal BMD and BUA on osteoporotic/osteopenic women and healthy controls. They found a higher correlation coefficient ($r = 0.79$) between calcaneal BMD and BUA than when BUA was correlated with other BMD sites. However, an earlier study by Glüer et al. (15) did not show improved correlations when BUA was site-matched with single X-ray absorptiometry. It is possible that changes in calcaneal QUS are more representative of BMD for other trabecular sites such as the lumbar spine than for cortical sites such as the femur.

Despite the moderate correlations of QUS to DXA, the literature shows that the potential use of QUS lies in its ability to predict hip fractures (3, 18, 22, 30), to discriminate osteoporotic individuals (1, 12, 16, 21, 25), and to detect the effect of load-

bearing exercise on bone health (8, 9, 26, 32). In a study by Schott (30), BUA significantly predicted hip fractures in elderly women after adjusting for BMD, despite low correlations between BMD and BUA. In addition, Kimmel et al. (22) found that QUS predicted stress fractures in a large cohort of female Army recruits during basic training. A study by Langton et al. (23) found moderate correlations between BMD and BUA, but a high sensitivity (77%) for BUA in identifying osteoporosis. They suggested the use of calcaneal BUA for selective screening of those meeting clinical criteria for risk of osteoporosis. They purported that those patients below a threshold value of BUA should be followed up with the more "precise" measurement of bone density by DXA (23, 25). These results exist independently of BMD. QUS has also been successful in determining the effect of exercise on bone presumably due to the sensitive response of the calcaneus to load-bearing activities. Taaffe et al. (32) showed that both BUA and regional and total body BMD were higher in young gymnasts (age 19) than in control subjects participating in regular weight-bearing activity. In a study on peripubertal girls, Lehtonen-Veromaa et al. (26) found that gymnasts and runners had higher QUS and BMD values than the non-athletic group. In addition, Jones et al. (20) found a significant increase in BUA after a year of an exercise intervention program. These studies show the validity of QUS is detecting disease, risk of fracture and the benefits of exercise. Therefore, the measurement of bone quality by QUS may be an important supplement to the measurement of BMD by DXA in determining an individual's overall bone health.

The results of this study also demonstrated that both BUA of the calcaneus and total body and regional BMD were significantly higher in men than in age-matched

women at the end of the third decade. Interestingly, the total spine and lumbar spine BMD were not significantly different between genders. Henry et al. (19) also showed significant gender differences in total body and femoral neck but not the lumbar spine. Other studies have reported gender differences in BMD (13) and BMC (28) as well, and it is thought that bone size or cross-sectional area accounts for these results (14, 19). The cross-sectional dimension of women's vertebrae is approximately 25% smaller than that of men (13). Henry et al. (19) found that the observed gender difference in femoral neck BMD was no longer significant after adjusting for body size. Because the compressive strength of the vertebrae is dependent upon cross-sectional area as well as bone mass, women have an inherent mechanical disadvantage compared to men as evidenced by the lower BUA and BMD reported in the present study.

CONCLUSION

Because our results showed moderate correlations and non-significant Kappa coefficients and AUC between BUA and BMD, QUS cannot be used as a substitute for assessing BMD by DXA. The QUS measures different qualities of bone in addition to BMD, which would explain the poor discriminative ability of QUS in this study. However, because the literature shows that BUA is sensitive to changes in bone due to exercise regime and can detect those at risk for fracture and osteoporosis, ultrasound cannot be ruled out as a tool for monitoring bone health. Prospective long-term studies are required to ascertain the role of ultrasound in assessing bone health in a young, active population.

REFERENCES

1. Agren M., A. Karellas, D. Leahey, S. Marks, and D. Baran. Ultrasound attenuation of the calcaneus: a sensitive and specific discriminator of osteopenia in postmenopausal women. *Calcif. Tissue Int.* 48: 240-244, 1991.

2. Almeida S. A., K. M. Williams, R. A. Shaffer, and S. K. Brodine. Epidemiological patterns of musculoskeletal injuries and physical training. *Med. Sci. Sports Exerc.* 31: 1176-1182, 1999.

3. Bauer D. C., C. C. Gluer, H. K. Genant, and K. Stone. Quantitative ultrasound and vertebral fracture in postmenopausal women. Fracture Intervention Trial Research Group. *J. Bone Miner. Res.* 10: 353-358, 1995.

4. Beck T. J., C. B. Ruff, F. A. Mourtada, R. A. Shaffer, K. Maxwell-Williams, G. L. Kao, D. J. Sartoris, and S. Brodine. Dual-energy X-ray absorptiometry derived structural geometry for stress fracture prediction in male U.S. Marine Corps recruits. *J. Bone Miner. Res.* 11: 645-653, 1996.

5. Bennell K. L., S. A. Malcolm, P. D. Brukner, R. M. Green, J. L. Hopper, J. D. Wark, and P. R. Ebeling. A 12-month prospective study of the relationship between stress fractures and bone turnover in athletes. *Calcif. Tissue Int.* 63: 80-85, 1998.

6. Cohen J. A coefficient of agreement for nominal scales. *Educ. Psychol. Meas.* 20: 37-46, 1960.

7. Dubois E. F. L., J. P. W. van den Bergh, A. G. H. Smals, C. W. D. van de Meerendonk, A. H. Zwinderman, and D. H. Schweitz. Comparison of quantitative ultrasound parameters with dual energy X-ray aborptiometry in pre- and postmenopausal women. *The Netherlands J. of Med.* 58: 62-70, 2001.

8. Etherington J., P. A. Harris, D. Nandra, D. J. Hart, R. L. Wolman, D. V. Doyle, and T. D. Spector. The effect of weight-bearing exercise on bone mineral density: a study of female ex-elite athletes and the general population. *J. Bone Miner. Res.* 11: 1333-1338, 1996.

9. Etherington J., J. Keeling, R. Bramley, R. Swaminathan, I. McCurdie, and T. D. Spector. The effects of 10 weeks military training on heel ultrasound and bone turnover. *Calcif. Tissue Int.* 64: 389-393, 1999.

10. Friedl K. E., J. A. Nuovo, T. H. Patience, and J. R. Dettori. Factors associated with stress fracture in young Army women: indications for further research. *Mil. Med.* 157: 334-338, 1992.

11. Frost M. L., G. M. Blake, and I. Fogelman. Does the combination of quantitative ultrasound and dual-energy X-ray absorptiometry improve fracture discrimination? *Osteoporos. Int.* 12: 471-477, 2001.

12. Frost M. L., G. M. Blake, and I. Fogelman. Quantitative ultrasound and bone mineral density are equally strongly associated with risk factors for osteoporosis. *J. Bone Miner. Res.* 16: 406-416, 2001.

13. Gilsanz V., M. I. Boechat, R. Gilsanz, M. L. Loro, T. F. Roe, and W. G. Goodman. Gender differences in vertebral sizes in adults: biomechanical implications. *Radiology* 190: 678-682, 1994.

14. Gluer C. C., M. Vahlensieck, K. G. Faulkner, K. Engelke, D. Black, and H. K. Genant. Site-matched calcaneal measurements of broad-band ultrasound attenuation and single X-ray absorptiometry: Do they measure different skeletal properties? *J. Bone Miner. Res.* 7: 1071-1079, 1992.

15. Gluer C. C., C. Y. Wu, M. Jergas, S. A. Goldstein, and H. K. Genant. Three quantitative ultrasound parameters reflect bone structure. *Calcif. Tissue Int.* 55: 46-52, 1994.

16. Greenspan S. L., M. L. Bouxsein, M. E. Melton, A. H. Kolodny, J. H. Clair, P. T. Delucca, M. Stek, Jr., K. G. Faulkner, and E. S. Orwoll. Precision and discriminatory ability of calcaneal bone assessment technologies. *J. Bone Miner. Res.* 12: 1303-13, 1997.

17. Greenspan S. L., S. Cheng, P. D. Miller, and E. S. Orwoll. Clinical performance of a highly portable, scanning calcaneal ultrasonometer. *Osteoporos. Int.* 12: 391-398, 2001.

18. Heaney R. P., L. V. Avioli, C. H. Chesnut, III, J. Lappe, R. R. Recker, and G. H. Brandenburger. Ultrasound velocity, through bone predicts incident vertebral deformity. *J. Bone Miner. Res.* 10: 341-345, 1995.

19. Henry Y. M. and R. Eastell. Ethnic and gender differences in bone mineral density and bone turnover in young adults: effect of bone size. *Osteoporos. Int.* 11: 512-517, 2000.

20. Jones P. R., A. E. Hardman, A. Hudson, and N. G. Norgan. Influence of brisk walking on the broadband ultrasonic attenuation of the calcaneus in previously sedentary women aged 30-61 years. *Calcif. Tissue Int.* 49: 112-115, 1991.

21. Kimmel D. B., R. P. Heaney, and L. V. Avioli. Patellar ultrasound velocity in osteoporotic and normal subjects of equal forearm or spinal bone density. *J. Bone Miner. Res.* 6: 175, 1991.

22. Kimmel D. B., J. M. Lappe, M. J. Laurin. Prediction of stress fracture risk during basic training in female soldiers by calcaneal ultrasound. *J. Bone Miner. Res.* 11: S110, 2001.

23. Langton C. M., P. A. Ballard, D. K. Bennett, and D. W. Purdie. A comparison of the sensitivity and specificity of calcaneal ultrasound measurements with clinical criteria for bone densitometry (DEXA) referral. *Clin. Rheumatol.* 16: 117-118, 1997.

24. Langton C. M. and D. K. Langton. Comparison of bone mineral density and quantitative ultrasound of the calcaneus: site-matched correlation and discrimination of axial BMD status. *Br. J. Radiol.* 73: 31-35, 2000.

25. Langton C. M., D. K. Langton, and S. A. Beardsworth. Comparison of accuracy and cost effectiveness of clinical criteria and BUA for referral for BMD assessment by DXA in osteoporotic and osteopenic perimenopausal subjects. *Technol. Health Care* 7: 319-330, 1999.

26. Lehtonen-Veromaa M., T. Mottonen, I. Nuotio, O. J. Heinonen, and J. Viikari. Influence of physical activity on ultrasound and dual-energy X-ray absorptiometry bone measurements in peripubertal girls: a cross-sectional study. *Calcif. Tissue Int.* 66: 248-254, 2000.

27. Metz C. E., B. A. Herman, and J. H. Shen. Maximum likelihood estimation of receiver operating characteristic (ROC) curves from continuously-distributed data. *Stat. Med.* 17: 1033-1053, 1998.

28. Nindl B. C., C. R. Scoville, K. M. Sheehan, C. D. Leone, and R. P. Mello. Gender differences in regional body composition and somatotrophic influences of IGF-I and leptin. *J. Appl. Physiol*. 92:1611-1618, 2002.

29. Rosenthall L., A. Tenenhouse, and J. Caminis. A correlative study of ultrasound calcaneal and dual-energy X-ray absorptiometry bone measurements of the lumbar spine and femur in 1000 women. *Eur. J. Nucl. Med.* 22: 402-406, 1995.

30. Schott A. M., S. Weill-Engerer, D. Hans, F. Duboeuf, P. D. Delmas, and P. J. Meunier. Ultrasound discriminates patients with hip fracture equally well as dual energy X-ray absorptiometry and independently of bone mineral density. *J. Bone Miner. Res.* 10: 243-249, 1995.

31. Siris E. S., P. D. Miller, E. Barrett-Connor, K. G. Faulkner, L. E. Wehren, T. A. Abbott, M. L. Berger, A. C. Santora, and L. M. Sherwood. Identification and fracture outcomes of undiagnosed low bone mineral density in postmenopausal women: results from the National Osteoporosis Risk Assessment.PG - 2815-22. *Jama* 286: 2815-22, 2001.

32. Taaffe D. R., C. Duret, C. S. Cooper, and R. Marcus. Comparison of calcaneal ultrasound and DXA in young women. *Med. Sci. Sports Exerc.* 31: 1484-1489, 1999.

33. Tromp A. M., J. H. Smit, D. J. Deeg,and P. Lips. Quantitative ultrasound measurements of the tibia and calcaneus in comparison with DXA measurements at various skeletal sites. *Osteoporos. Int.* 9: 230-235, 1999.